

cal symptoms of the disease are present along with hyperglycemia or even glycosuria, a tolerance test is altogether unnecessary. The test is valuable, however, where suggestive symptoms of the disease occur in the absence of glycosuria. High renal thresholds in true diabetics, especially in old patients, are not uncommon. The meaning of a definite glycosuria in the absence of any symptoms of diabetes mellitus, moreover, must often be determined by the glucose tolerance test. Our series of curves in normal students again reveals the occurrence of intermittent glycosuria in normal people. Renal diabetes with continuous glycosuria due to a low kidney threshold is not uncommon, and its diagnosis is made possible by the tolerance test.

For the present, we must depend on the standard glucose test for our diagnostic data. A palatable carbohydrate meal, however, would certainly be a more normal load than 100 grams of glucose. If such a carbohydrate meal ever supplants the glucose meal, it will be necessary to determine the optimal amount of mixed carbohydrate that will furnish the proper strain on the pancreas to reveal a true diabetic tendency. Our study of the 50-gram starch meal indicates that it is too light a load to detect mild types of this disease. Until more work of this type has been done with larger amounts of mixed carbohydrate food, we must continue to use the standard glucose test in our investigation of questionable causes of diabetes mellitus.

### SOME CERTAIN CONSIDERATIONS IN TREATING THE MENOPAUSE†

By LUDWIG A. EMGE \*

DISCUSSION by H. Lissner, San Francisco.

WITH the advent of endocrinology and organotherapy it was generally expected that a complete revolution would occur in the treatment of the menopause. There was an outburst of organotherapeutic enthusiasm carefully nursed along by semicommercial literature. Then came a wave of disappointment and the clearer thinkers in the profession began to counsel against the indiscriminate use of organic preparations. We are now in the negative phase, and skepticism threatens to bring into disrepute one very valuable but no infallible agent in the treatment of the menopause.

It is needless for me to repeat the well-known symptomatology of the menopause. I shall confine myself to a few remarks on the vasomotor and biochemical phenomena studied during the last few years.

**Blood Pressure**—Changes are common but definite percentages are difficult to arrive at, because the menopausal age and the common hypertension age, due to pathologic changes, occur at about the same period in life. In the absence of demonstrable or-

ganic lesions hypertension should be transient, as readjustment of the endocrine factors controlling the vasomotor nervous system takes place. If blood pressure equalization does not occur at the cessation of other menopausal symptoms it is safe to assume that undiscovered organic disease exists. From the literature and my own observation I judge that about 40 to 45 per cent of women in the menopause have hypertension, 5 to 10 per cent of whom will approach a blood pressure of 200 mm.; 40 per cent remain unchanged and from 10 to 15 per cent have hypotension. Shifting from one to the opposite extreme has been repeatedly observed.

**Metabolism**—Observations are still quite few in number. Basal metabolism studies made during either the artificial or normal menopause suggest that approximately 55 per cent of women have a lowered metabolic rate, 30 per cent remain unchanged, and 15 per cent show a rate above normal.

**Blood Calcium**—It is known that in osteomalacia in women progressive calcium loss can be arrested by castration. Hence it has been assumed that certain ovarian functions have a close affinity to the calcium exchange of the body. During the menopause calcium commonly is increased if we may go by the few reports on record. This change seems to follow the removal of the inhibiting ovarian hormone to the adrenal, hypophysis or thyroid glands. The subject has been studied indirectly in idiopathic climacteric menorrhagia which by injections of calcium chloride has been markedly benefited. The German literature has persistently reported good results after the use of other forms of calcium given together with sedatives or ovarian preparations in the treatment of menopausal vasomotor disturbances due to sympathetic irritability. Assuming that these clinical observations stand undisputed for the present, we may deduce that calcium metabolism and irritability of the sympathetic nervous system are closely related.

**Endocrine Relations**—While our knowledge is fragmentary and theoretical in many respects, we have at least some definite factors which repeat themselves quite regularly. We know that the Graafian follicular apparatus disappears quite rapidly as a consequence of which atrophy of the generative organs and amenorrhea occur. This is followed by hypertrophic phenomena in the secondary sex glands, i. e., thyroid, hypophysis, and adrenals. This hypertrophy usually manifests itself in one gland and most often in one constituent of this gland. Thus, it is only the cortex of the adrenal gland which hypertrophies. In the hypophysis it commonly is the pars anterior, while in the thyroid a general hypertrophy is seen. It is this peculiar shifting of the endocrine balance which is responsible for a host of different manifestations in different individuals. If one gland alone compensates for the ovarian loss the end-manifestation is usually quite apparent. Thus, we speak of such types as the pituitary or thyroid types, either of which may again be expressed in a hyper- or hypofunction type. In other words, a tertiary action takes place in which the increased influence of the hypertrophic gland leads to an inhibition of another gland manifesting itself in hypofunction. Consid-

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ered as a whole our problem is a pluriglandular one, although basically it must be regarded as a monoglandular question. The difficulty arises in the determination of the pivotal gland. We have similar problems in amenorrhea of earlier ages. For instance, in hyperthyroidism the overactive thyroid inhibits the ovaries producing secondary amenorrhea. While in myxedema the hypophysis enlarges producing a tertiary amenorrhea. The lack of time prevents me from going further into this question. While we do not know anything of the origin of primary ovarian inhibition ushering in the climacterium, we have some basic information of the processes that follow. Based on the latter a fairly successful organotherapy combined with proper hygiene and some symptomatic therapeutics offers a reasonable outlook for success in the treatment of the menopause. There is no doubt in my mind that the greatest success in treating any form of the menopause is reached by a proper management of the patient during its early phases. If we could teach women to recognize this fact we would thereby remove a serious stumbling block to therapeutic success.

Since our knowledge of the endocrine dynamics of the menopause is still so very fragmentary, it is obviously impractical to lay down definite rules for an endocrine treatment. At best, we must content ourselves for the present to differentiate between certain general types of menopausal changes which may represent either thyroid or pituitary or adrenal dysfunctions. In observing this rule we shall find a fair amount of guidance for a more rational utilization of organic preparations. Where types overlap, pluriglandular treatment may become necessary but should at all times be considered as a last resort. It has been my experience that a large majority of menopausal women respond to monoglandular therapy. Since the predominance of one gland may be displaced or overshadowed by another during the progress of the menopause, it is obvious that different types of glandular preparations may have to be substituted for each other.

Theoretically, the ovarian preparations should fill all of the demands of endocrine deficiencies during the menopause. Practical experience has taught us that this is not the case. To my knowledge only vasomotor instability and nervous irritability, when not accompanied by change in blood pressure, will respond readily to either ovarian residue or whole ovary. Apparently the adrenal glands are thus balanced and sympathetic irritation is removed. Thyroid extract is to be utilized when there is low blood pressure, mental depression, and lowered metabolism. It is obvious that this substance should not be used when the opposite condition exists. Corpus luteum is most helpful in hypertension. It should not be forgotten that this substance antagonizes the thyroid gland. It also stimulates the pituitary gland and hence is of value in pituitary depression. Direct pituitary stimulation through pituitary preparations is still very unsatisfactory. At times pituitary disturbances seem to respond well to a combination of whole ovary and thyroid extracts.

There is no standard dosage for any of the organic preparations used in the treatment of the meno-

pause. With the exception of thyroid none of these substances is standardized. Hence one must feel one's way by starting with small doses and rapidly increasing them to the point of functional saturation. I am not at all convinced that much is to be gained by hypodermic medication in preference to medication by mouth. Fresh dried organic extracts protected against deterioration, especially when they are put up in glycerine, seem to give as much and often more satisfaction than hypodermic preparations. They have the added advantage of less discomfort and less expense to the patient. A great deal of dissatisfaction has arisen from the use of shopworn and indifferent preparations. There is no doubt that available products differ materially in active principles in one given preparation. It is therefore most essential that one acquaint oneself with the true equivalent of the fresh substance contained in the commercial article. Consequently one should specify precisely the make of the substance to be used. By keeping careful records one can soon find out what substances are most suitable and serviceable. Next, close supervision of the patient with regard to blood pressure and visible body changes will prevent any misdirected effort should shifting of the endocrine balance take place.

Recently calcium, at times combined with theobromine, has been advocated as an important adjunct to ovarian organotherapy. My experience with it is still too limited to express an opinion as to the value of this method. What I have seen seems to substantiate the claims set forth in the literature.

Some very interesting reports on the radiological treatment of the menopause come from Germany. According to the type of the endocrine dysfunction either the thyroid or the pituitary gland is exposed to given doses of x-ray. Astonishing results are claimed for this treatment in which the psychic factor has been definitely eliminated by proper experiments. As far as I can learn from the literature this treatment has not been used elsewhere. If the claims made for it can be substantiated it will displace organotherapy in either the artificial or normal menopause.

In spite of our best efforts we find only too often that organotherapy alone will not solve our problem. We then have to fall back on the time-honored remedies of an earlier period. Among them valerian preparations seem to be the most helpful. Proper body and mental hygiene should always have a prominent part in the treatment of the menopause regardless of what other course of treatment is pursued.

There are a great many other aspects of the menopause that are most interesting, but they must be left to another discussion. In leaving the subject I once more caution against the indiscriminate use of the extracts of endocrine glands. They are not infallible in their action nor are they fool-proof in the hands of the careless. Notwithstanding the opinion of a few well-known observers who dispute any merit of this method of treatment, I have learned from personal experience that sensible organotherapy is a most helpful agent in the treatment of the menopause.

## DISCUSSION

H. LISSER, M. D. (Fitzhugh Building, San Francisco)—Doctor Emge can always be counted upon to present a sane and conservative viewpoint; this paper is no exception. With brevity and clarity he has presented the essential facts as far as present knowledge permits.

The matter of endocrine control of calcium metabolism has acquired a renewed and more precise interest since the remarkable work of Collip, who has perfected a potent parathyroid extract (now available as "Parathormone"). This extract has a specific and profound effect in raising the blood serum calcium; it mobilizes calcium; it is only effective by injection. Tetany is a state of hypoparathyroidism and is accompanied by a strikingly diminished blood serum calcium. The most characteristic phenomenon of this incretory disease is increased excitability of the entire nervous system, motor, sensory, psychic and vasomotor. It seems a bit contradictory therefore to assume an increased calcium content after the menopause and hold it responsible for vasomotor excitability. Calcium determinations must be performed with scrupulous accuracy; perhaps previous observations have been incorrect. At any rate if any noteworthy disturbance in calcium balance attaches to the menopause, the *modus operandi* is probably an indirect one through derangement of parathyroid function. There is a hint here for interesting clinical experimentation.

The artificial menopause is apt to be more severe than the natural climacteric, probably because it is so abrupt, and the earlier it is produced the more violent are the symptoms. Indeed these may be so distressing as to cause utter wretchedness and incapacity. The severer the symptoms the less efficacious the remedies. Surgeons cannot be warned too strongly to spare the ovaries wherever possible, especially in young women. Carelessness in this matter is positively reprehensible.

Not long ago I attempted to classify the various commercial preparations according to their merits. In Class A were grouped those extracts which were standardized and potent, namely, thyroid, insulin, parathormone, adrenalin (from the adrenal medulla) and pituitrin (from the posterior hypophysis). Class B included extracts which were worth while but inconsistent; Class C comprised those which were deemed practically worthless. Ovarian extracts were assigned to Class B. Rapid strides are being made in the biochemical investigation of glandular extracts; only a few years ago parathyroid and pancreatic extracts would have been ignominiously dumped into Class C. Indeed there are important developments in the study of ovarian products, notably by Allen and Doisy of St. Louis, and the Denver group of Frank Gustavson, etc.

We may confidently look forward to a more satisfactory ovarian therapy before very long. In the meantime we must do the best we can with the methods Emge has outlined.

**Infantile Tetany**—Twenty-one cases of infantile tetany have been studied by John P. Scott, Philadelphia, and Saul J. Usher, Montreal (*Journal A. M. A.*). They found that calcium chloride and ammonium chloride were specific in relieving the convulsions of tetany as long as they were given. In one case, when the calcium chloride was discontinued, even for a day, the convulsions reappeared. Furthermore the signs of latent tetany, such as the Chvostek and Trousseau signs, were found present even after several weeks' administration of either salt. In the main, there was an appreciable elevation of the blood calcium after the giving of either salt, but in two cases there was a definite lowering. Cod liver oil in large doses, when combined with calcium chloride, or by itself, slowly and permanently raised the blood calcium into the normal range. Ultraviolet ray treatment gave the most rapid restoration of the blood calcium to normal figures. Frequent treatments with the mercury vapor quartz lamp give the quickest and most permanent results. Both the tetany and the accompanying rickets are cured. The ultraviolet rays raise the calcium concentration and also that of the inorganic phosphorus to normal by causing increased absorption of these elements from the gastrointestinal tract.

## URETERAL REFLUX

By JAMES R. DILLON \*

*The possible conditions of reflux in my patients seem to be associated more with urinary infection and pathological conditions of the kidney than with urethral obstruction.*

*Utilizing the principles of gravity, ureteral backflow and bladder distention, producing a hypertonicity of the bladder musculature will greatly aid in obtaining good pyeloureterograms in patients hard to catheterize or with overactive ureteral peristalsis.*

*The possible use of ureteral reflux in the treatment of bilateral pyelitis instead of kidney lavage in patients where reflux is found to exist is indicated.*

*Reflux undoubtedly plays an important part in carrying infection of the lower urinary tract to the upper, and possibly from a diseased kidney to a normal one, and we should use more caution in the treatment of patients with cystitis.*

DISCUSSION by Louis Clive Jacobs, San Francisco; L. P. Player, San Francisco.

MANY articles have appeared in the last few years calling our attention to the condition of ureteral reflux, or backflow of bladder urine into the ureters to the kidney pelves. This phenomenon has been studied from the clinical and animal experimental standpoints, both as to its occurrence in establishing the fact of ascending infection of the kidneys and its treatment, but little has been mentioned as to the practical use that may be made of it in urology.

Most of the reports in the literature have been on the occasional accidental observation of reflux in the taking of cystograms and has generally been associated with pathological conditions, as shown by Bumpus in a study of 1036 cystograms, finding it in one or both ureters in eighty-nine pathological cases, or 8½ per cent. Braash and Draper, who made an experimental study on dogs in doing meatotomies on the ureteral orifices concluded that the peristaltic action of the ureter was sufficient to protect the kidney even if the ureterovesical valve was destroyed, and that "renal infections are seldom if ever ascending, but rather hematogenous in origin."

Graves and Davidoff found it occurred in 73 per cent of a large number of normal rabbits, and in 78 per cent where the ureters had been rendered abnormal by previous operative procedures. They conclude that the phenomenon of reflux depends primarily upon the sustained tonus of the bladder musculature as it actively resists distention; and that the ureterovesical valve and ureteral peristalsis are insufficient protections "against the ascent of accumulating bladder contents into the ureters in the presence of an actively contracting bladder with vesical neck obstruction." Also they did not see antiperistalsis in any normal ureter and found it in no way concerned with regurgitation.

My experimental work with the assistance of Dr. B. A. Cody on normal animals has been along the lines practiced in the treating of bladder conditions and the making of urological examinations on the human, with no attempt to attain the hyper-

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